

# CERTIFICATE OF ANALYSIS

Material : <b>MELPHALAN</b>	Certificate no. : <b>43647</b> Material no.: <b>3860300</b> Date of issuance : <b>24-Sep-2018</b>
Batch no.: <b>1801357</b>	Page 1 of 4

Supplier : ASPEN GLOBAL INCORP.  
 Supplierlotno. : 16-385-072  
 Manufacturer : AMPAC Fine Chemicals, California, USA  
 Packaging : Kunststoffbehälter (WE)

Retest date : 11-Jul-2018  
 Expiry date: 11-Jul-2018  
 Specification : PQQ00/699/09/3

Monograph:	Ph.Eur.	Melphalan	8.0
	BP	Melphalan	2016

Characteristics : white to almost white hygroscopic powder

Remarks :

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Mat. no.	Description	Batch	Testprotocol
3860300	MELPHALAN Specification : PQK00/699/09/3	1801357	1847786
Parameter	Limit	Result	Lab.
<b>Organisation</b>			
Content for production		96.8 %	Excella
<b>Characteristics</b>			
Colour	Complies	Complies	Excella
<b>Identity</b>			
IR spectrum	Complies	Complies	Excella
Identity HPLC	Complies	Complies	Excella
Chloride (JP)	Chloride (JP)	Complies	Excella
<b>Characteristic values</b>			
Specific rotation	-36.0 ... -30.0 °	-35.0 °	Excella
<b>Purity</b>			
Water (KF)	Max. 5.0 %	1.7 %	Excella
Total volatiles	Max. 7.0 %	1.7 %	Excella
Chloride (in 0,1 M AgNO3)	Max. 1.0 ml	0.1 ml	Excella
Sulphated ash	Max. 0.1 %	< 0.1 %	Excella
Heavy metals (JP)	Max. 20 ppm	< 20 ppm	Excella
Arsenic (JP)	Max. 2 ppm	< 2 ppm	Excella
Loss on drying (JP)	Max. 7.0 %	1.4 %	Excella
<b>Related compounds LC</b>			
Dihydroxymelphalan	Max. 0.10 %	< 0.01 %	Excella
Morpholino derivative	Max. 0.3 %	< 0.1 %	Excella
Mono-(2-chloroethyl)aminomelphalan	Max. 0.10 %	0.01 %	Excella
Monohydroxymelphalan	Max. 3.0 %	0.5 %	Excella
2-Methoxyethylmelphalan	Max. 0.2 %	< 0.1 %	Excella
Chloroethoxymelphalan	Max. 0.5 %	0.1 %	Excella
3-Chloromelphalan	Max. 0.10 %	0.01 %	Excella
Melphalan dimer	Max. 1.0 %	0.8 %	Excella
Melphalan methyl ester	Max. 0.5 %	< 0.1 %	Excella
unknown single	Max. 0.10 %	0.04 %	Excella
total	Max. 5.5 %	1.5 %	Excella
<b>Residual solvents</b>			
Methanol	Max. 2.5 %	< 0.1 %	Excella
Diethylamine	Max. 0.5 %	< 0.1 %	Excella
Benzene	Max. 1 ppm	< 1 ppm	Excella

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Mat. no.	Description	Batch	Testprotocol
3860300	MELPHALAN Specification : P Q K 0 0 / 6 9 9 / 0 9 / 3	1801357	1847786
Parameter	Limit	Result	Lab.
<b>Particle size</b>			
Sieve residue 250 µm	Max. 10 %	0 %	Excella
particle size d(10)	Max. 4 µm	3 µm	Excella
particle size d(50)	5 ... 40 µm	12 µm	Excella
particle size d(90)	Max. 100 µm	68 µm	Excella
<b>Assay</b>			
HPLC	95.0 ... 100.5 %	98.5 %	Excella
<b>Purity</b>			
Palladium	Max. 10 ppm	< 1 ppm	Supplier

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The material was tested under current GMP requirements.  
The material was tested according to the current test procedures.  
Batch 1801357 complies with the specification.

Conditions / comment :
Certified retest date from supplier Certificate passed. Released for immediate use after retest at Excella.

Disposition Status :	released by:	Release date :
Released	Eichhorn, Udo Manager Quality Control Pharma	14-Jun-2018



## Certificate of Analysis / Compliance

### Melphalan Milled

4-[Bis-(2-chloroethyl)amino]-L-phenylalanine

Lot Number 16-385-072

Manufacture Date 09 September 2016

Retest Date 09 September 2017

Batch Net Weight 4.305 kg

AGI Material Code: G20041

Aspen Global Inc. P.O. # 91000669

Test	Specifications	Results
Appearance	White or almost white hygroscopic powder	White Hygroscopic Powder
Identification by FTIR	Concordant with IR Reference Standard	Conforms
Identification by HPLC	Concordant with HPLC Reference Solution	Conforms
Identification - Chloride (JP)	Positive Qualitative Tests for Chloride	Conforms
Ionisable Chlorine (JP)	NMT 1.0 mL of 0.1M AgNO <sub>3</sub> per 0.5g	0.1 mL
Heavy Metals (JP)	NMT 20 ppm	< 20 ppm
Arsenic (JP)	NMT 2 ppm	< 2 ppm
Optical Rotation	-36.0 ° to -30.0 °	-34.2 °
Water Content by Karl Fischer	NMT 5.0%	1.2%
Loss on Drying (JP)	NMT 7.0 % w/w	0.8%
Sulfated Ash	NMT 0.1% w/w	0.0%
Non Aqueous Solvents		
Methanol	NMT 2.5% w/w	Not Detected
Impurity K (Diethylamine)	NMT 0.5% w/w	0.01%
Benzene	NMT 1 ppm	Not Detected

AMPAC Fine Chemicals

P.O. Box 1716 • Rancho Cucamonga, California 91767  
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www.ampacfinechemicals.com

AFC-COA-0385.07





## Certificate of Analysis / Compliance

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Lot Number 16-385-072

Manufacture Date 09 September 2016

Retest Date 09 September 2017

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AGI Material Code: G20041

Aspen Global Inc. P.O. # 91000669

Test	Specifications	Results
Total Volatiles including water	NMT 7.0% w/w	1.3%
Particle Size Sieve through 250 µm	NLT 90% w/w	100%
<u>Particle Size by Laser Sizer</u>		
Particle Size at x 10%	NMT 4µm	4 µm
Particle Size at x 50%	5 to 40 µm	16 µm
Particle Size at x 90%	NMT 100µm	75 µm
<u>Related Substances</u>		
Impurity A (Dihydroxymelphalan)	NMT 0.10%	Not Detected
Impurity B (Morpholino derivative)	NMT 0.3%	Not Detected
Impurity C (Mono-(2-chloroethyl)-aminomelphalan)	NMT 0.10%	Not Detected
Impurity D (Monohydroxymelphalan)	NMT 3.0%	0.46%
Impurity E (3-Chloromelphalan)	NMT 0.10%	0.01%
Impurity G (Melphalan dimer)	NMT 1.0%	0.58%
Impurity H (Melphalan methyl ester)	NMT 0.5%	Not Detected
Impurity I (2-Methoxyethylmelphalan)	NMT 0.2%	0.01%
Impurity J (Chloroethoxymelphalan)	NMT 0.5%	0.05%
Unknown Impurity	NMT 0.10%	RRT 0.44, 0.01% RRT 0.65, 0.03% RRT 0.71, 0.01% RRT 0.78, 0.01% RRT 1.13, 0.02% RRT 1.39, 0.01%
Total Impurities	NMT 5.5%	1.2%

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AGI Material Code: G20041

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Test	Specifications	Results
<u>Assay</u>		
Melphalan Volatiles Free	95.0 - 100.5% w/w	97.8%
Assay As Is	Report Results	96.5%
Parts per 100 Parts Melphalan	Report Results	104 parts per 100 parts Melphalan
Palladium Content by ICP-OES	NMT 10 ppm	< 1 ppm

It is hereby certified that the above product is acceptable under the requirements of the applicable product specification.

*James H. Kelly*  
Quality Control Laboratory

*11/21/16*  
Date

This is to certify that the above product meets the requirements of the Purchase Order. The Product was manufactured in conformance to applicable AFC procedures and the requirements for good manufacturing practices as recommended by the United States Food & Drug Administration. This batch has been manufactured, packaged and tested in accordance with EU GMP Guideline Volume 4 Part II (ICHQ7). This lot is approved and released for distribution.

*David L. Gentry*  
Quality Assurance

*11/21/16*  
Date